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Docket No. 55293-B-PCT-US/JPW/AJM/MVM

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Carlos Cordon-Cardo et al.

Serial No.: 10/009,861 Examiner: Not Yet Known

Filed : December 10, 2001 Group Art Unit: 1645

For : MARKERS FOR PROSTATE CANCER

1185 Avenue of the Americas
New York, New York 10036
February 28, 2003

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

TECH CENTER 1600/2900

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following references which are listed on Form PTO-1449 (**Exhibit A**).

1. PCT International Application No. PCT/US98/14566, filed July 14, 1998, International Publication No. WO99/04238, published January 28, 1999;
2. PCT International Application No. PCT/US98/01922, filed January 29, 1998, International Publication No. WO98/33450, published August 6, 1998;
3. PCT International Application No. PCT/US94/03528, filed March 30, 1994, International Publication No. WO94/22478 A, published October 13, 1994;
4. PCT International Application No. PCT/US98/26266, filed

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Page 2

December 10, 1998, International Publication No. WO99/31140 A,
published June 24, 1999;

5. Aaltomaa, S. et al. (1999) "Prognostic Value and Expression of p21 (waf1/cip1) Protein in Prostate Cancer" *The Prostate*, 39(1):8-15;
6. Agus, D.B. et al. (1999) "Response of Prostate Cancer to Anti-HER-2/neu Antibody in Androgen Dependent and -Independent Human Xenograft Models" *Cancer Research*, 59(1):4761-4764;
7. Arai, Y. et al. (1997) "C-erbB-2 Oncoprotein: A Potential Biomarker of Advanced Prostate Cancer" *Prostate*, 30(3):195-201;
8. Baretton, G.B. et al. (1999) "Proliferation- and Apoptosis-Associated Factors in Advanced Prostatic Carcinomas Before and After Androgen Deprivation Therapy: Prognostic Significance of p21/WAF1/CIP1 Expression" *British Journal of Cancer*, 80(3-4):546-555;
9. Baselga, J. et al., (1998) "Recombinant Humanized Anti-HER2 Antibody (Herceptin TM) Enhances the Antitumor Activity of Paclitaxel and Doxorubicin Against HER2/neu Overexpressing Human Breast Cancer Xenografts" 58(13):2825-2831;
10. Cariou S. et al. (1998) "Prognostic Implication of Expression of the Cell Cycle Inhibitor Protein P27", *Breast Cancer Research and Treatment*, 1-3(52):29-41;

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11. Cordon-Cardo Carlos, et al. (1998) "Distinct Altered Patterns of p27^{Kip1} Gene Expression in Benign Prostatic Hyperplasia and Prostatic Carcinoma" *J. Natl. Cancer Inst.* 90(17): 1284-1291;
12. Cote, R.J. et al. (1998) "Association of p27^{Kip1} Levels With Recurrence and Survival in Patients With Stage C Prostate Carcinoma" *J. Natl. Cancer Inst.* 90(12): 916-920;
13. Chen, Y. et al. (1998) "Increased Cell Growth and Tumorigenicity in Human Prostate LNCaP Cells by Overexpression to Cyclin D1" *Oncogene*, 16(15):1913-1920;
14. Craft, N. et al., (1999) "A Mechanism for Hormone-Independent Prostate Cancer Through Modulation of Androgen Receptor Signaling by the HER-2/neu tyrosine Kinase" *Nature Medicine*, 5(3):280-285;
15. Curnow, R.T. et al., (1997) "Clinical Experience With CD64-Directed Immunotherapy. An Overview" *Cancer Immunology And Immunotherapy*, 45(3-4):210-15;
16. Database Biosis [Online] Biosciences Information Service, Philadelphia, PA, US (1999-03) Lee Tae Yoon et al., "Immunohistochemical Expression of p53 and MDM-2 Protein in Various Epithelial Carcinomas" Database Accession No. PREV1999900406745;
17. DeMarzo, A.M. et al. (1998) "Prostate Stem Cell Compartments:

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Expression of the Cell Cycle Inhibitor p27kip1 in Normal, Hyperplastic, and Neoplastic Cells" *Amer. J. Path.* 153(3): 911-919;

18. Fernandez, P.L. et al. (1999) "Expression of p27kip1 Is Down-regulated in Human Prostate Carcinoma Progression" *J. Path.* 187 (5): 563-566;
19. Gumbiner, L. et al. (1999) "Overexpression of Cyclin D1 Is Rare in Human Prostate Carcinoma" *Prostate*, 38(1):40-45;
20. Guo, Y. et al. (1997) "Loss of the Cyclin-dependent Kinase Inhibitor p27^{Kip1} Protein in Human Prostate Cancer Correlates with Tumor Grade¹" *Clin. Cancer Res.* 3:2269-2274;
21. Han, E. et al., (1998) "Cyclin D1 Expression in Human Prostate Carcinoma Cell Lines and Primary Tumors" *Prostate*, 35(2):95-101;
22. James, N. et al., (1998) "Phase II Trial of the Bispecific Antibody MDX-H210 (Anti-Her2/Neu X Anti-CD64) Combined With GM-CSF In Patients With Advanced Prostate and Renal Cell Carcinomas That Express Her2/Neu" *British Journal of Cancer*, 78(Suppl 2):19;
23. Koeneman, K.S. et al., (1999) "Osteomimetic Properties of Prostate Cancer Cells: A Hypothesis Supporting the Predilection of Prostate Cancer Metastasis and Growth in the Bone Environment" *Prostate*, 39:246-261;

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24. Lee, C.T. et al., (1999) "Overexpression of the Cyclin-Dependent Kinase Inhibitor P16 is Associated with Tumor Recurrence in Human Prostate Cancer" *Clinical Cancer Research, The American Association for Cancer Research, US*, 5(5):977-983;
25. Lloyd et al. (1999) "P27^{kip1}: a Multifunctional Cyclin-dependent Kinase Inhibitor with Prognostic Significance in Human Cancers" *American J. Pathology* 154(2): 313-323;
26. McArthur, J.G. et al. (1999) "Cancer Gene Therapy with Novel Chimeric P27/p16 Tumor Suppressor Genes" *Proceed. Amer. Assoc. Cancer Res. Ann.* 40: 630;
27. Osman, I. et al. (1999) "Inactivation of the p53 Pathway in Prostate Cancer: Impact on Tumor Progression" *Clinical Cancer Research: An Official Journal of the American Association for Cancer Research*, 5(8):2082-2088;
28. Ross, J.S. et al., (1993) "Contribution of HER-2/neu Oncogene Expression to Tumor Grade and DNA Content Analysis in the Prediction of Prostatic Carcinoma Metastasis" *Cancer*, 72(10):3020-3028;
29. Veltri, R. et al. (1994) "Quantitative nuclear morphometry, Markovian Texture Descriptors, and DNA content Captured on a CAS-200 Image Analysis Systems, Combined With PCNA and HER-2/neu Immunohistochemistry for Prediction of Prostate Cancer

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Progression" *Journal of Cellular Biochemistry*, 19:249-258;

30. Yamasaki, I. et al. (1996) "Overexpression of MDM2 and p53 Protein is Infrequently but Significantly Associated With Progression of Human Prostatic Adenocarcinoma" *Oncology Reports*, 3(5):925-929; and
31. Zhau, H. et al. (1992) "Expression of C-erb B-2/neu Proto-Oncogene in Human Prostatic Cancer Tissues and Cell Lines" *Molecular Carcinogenesis*, 5(4): 320-327.

The subject application is a §371 national stage application and claims the benefit under 35 U.S.C. §120 of PCT International Application No. PCT/US00/16007, filed June 9, 2000, which is a continuation-in-part and claims benefit under 35 U.S.C. §120 of U.S. Serial No. 09/329,917, filed June 10, 1999.

The above-listed references 2, 5-11, 13, 15-20 and 23-30 were submitted to and considered by the United States Patent and Trademark Office in an Information Disclosure Statement filed on May 23, 2000 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. Also, above-listed reference 1 was cited by the United States Patent and Trademark Office in a Final Office Action dated December 20, 2001 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. Accordingly, under 37 C.F.R. §1.98(d) copies of these references are not required to be provided to the United States Patent and Trademark Office, since they were previously submitted to or cited by the United States Patent and

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Trademark Office in an application relied upon for an earlier filing date under 35 U.S.C. §120.

A Supplementary Partial European Search Report was issued on November 29, 2002 in connection with European Application No. EP 00938256.5, which is a related foreign counterpart of the subject application. A copy of the Supplementary Partial European Search Report is attached hereto as **Exhibit B**. Above-listed references 1-31 were cited in the Supplementary Partial European Search Report. References 6, 11-12, 20, 24 and 27 were submitted to and considered by the United States Patent and Trademark Office in an Information Disclosure Statement filed on May 23, 2000 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. Reference 25 was submitted to and considered by the United States Patent and Trademark Office in a Supplemental Information Disclosure Statement filed on December 19, 2000 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. References 1-2, 17-18 and 26 were submitted to and considered by the United States Patent and Trademark Office in a Supplemental Information Disclosure Statement filed on October 10, 2002 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. References 3-5, 7-10, 13-16, 19, 21-23 and 28-31 are being submitted concurrently to the United States Patent and Trademark Office in a Supplemental Information Disclosure Statement filed on February 28, 2003 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. Accordingly, under 37 C.F.R. §1.97(d), copies of these references are not required to be provided to the United States Patent and Trademark Office, since they were, or are being concurrently submitted herewith, whichever is applicable, to the United States Patent and Trademark Office in an application relied upon for an earlier filing date under 35

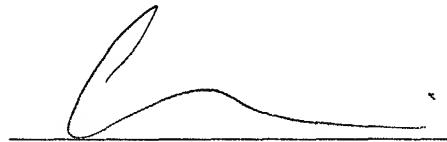
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U.S.C. §120.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Alan J. Morrison
Registration No. 37,399
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• 2/28/03
Alan J. Morrison
Reg. No. 37,399

Date

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U.S. PATENT DOCUMENTS

Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Subclass	Translation	
						Yes	No
	WO 9 9 0 4 2 3 8	1/28/99	PCT				
	WO 9 8 3 3 4 5 0	5/6/98	PCT				
	WO 9 4 2 2 4 7 8	10/13/94	PCT				
	WO 9 9 3 1 1 4 0	6/24/99	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Aaltomaa, S. et al. (1999) "Prognostic Value and Expression of p21 (waf1/cip1) Protein in Prostate Cancer" <i>The Prostate</i> , 39(1):8-15;
	Agus, D.B. et al. (1999) "Response of Prostate Cancer to Anti-HER-2/neu Antibody in Androgen Dependent and -Independent Human Xenograft Models" <i>Cancer Research</i> , 59(1):4761-4764;
	Arai, Y. et al. (1997) "C-erbB-2 Oncoprotein: A Potential Biomarker of Advanced Prostate Cancer" <i>Prostate</i> , 30(3):195-201;
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this from with next communication to applicant.

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 Exhibit A

Form PTO-1449

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	Cariou S. et al. (1998) "Prognostic Implication of Expression of the Cell Cycle Inhibitor Protein P27", <i>Breast Cancer Research and Treatment</i> , 1-3(52):29-41;
	Cordon-Cardo Carlos, et al. (1998) "Distinct Altered Patterns of p27 ^{Kip1} Gene Expression in Benign Prostatic Hyperplasia and Prostatic Carcinoma" <i>J. Natl. Cancer Inst.</i> 90(17): 1284-1291;
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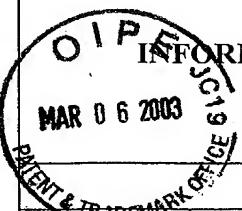
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E. GUTMANN - Y. PLASSERAUD S.A.

Datum/Date

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Zeichen/Ref./Réf. B5149 - CA	Anmeldung Nr./Application No./Demande n°./Patent Nr./Patent No./Brevet n°. 00938256.5
Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire Sloan-Kettering Institute For Cancer Research	

COMMUNICATION

The European Patent Office herewith transmits

- the European search report
- the declaration under Rule 45 EPC
- the partial European search report under Rule 45 EPC
- the supplementary European search report concerning the international application under Article 157(2) EPC relating to the above-mentioned European patent application. Copies of the documents cited in the search report are enclosed.

The following specifications given by the applicant have been approved by the Search Division :

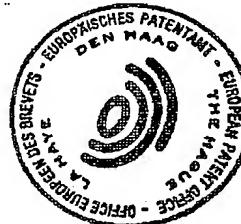
Abstract Title Figure

The abstract was modified by the Search Division and the definitive text is attached to this communication.

The following figure will be published with the abstract, since the Search Division considers that it better characterises the invention than the one indicated by the applicant.

Figure:

Additional copy(copies) of the documents cited in the European search report.



REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.

EPO Form 1507 02.93

Applicants: Carlos Cordon-Cardo et al.

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Exhibit B



European Patent
Office

Application Number
EP 00 93 8256

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):

- No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

- As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

- Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

- None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:



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**LACK OF UNITY OF INVENTION
SHEET B**

Application Number

EP 00 93 8256

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-4, 6-9, 11-12, 26-27

Methods, uses, and compositions relating to p27.

2. Claims: 14, 28

Methods and use relating to p21.

3. Claims: 15, 29

Methods and use relating to mdm2.

4. Claims: 16-17, 30

Methods and use relating to cyclin D1.

5. Claims: 18, 31

Methods and use relating to p16.

6. Claims: 19-25

Uses and methods relating to Her-2/neu.



European Patent
Office

SUPPLEMENTARY
PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention EP 00 93 8256
shall be considered, for the purposes of subsequent
proceedings, as the European search report

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	WO 99 04238 A (DRAETTA GIULIO ;MITOTIX INC (US); LODA MASSIMO (US); PAGANO MICHEL) 28 January 1999 (1999-01-28)	1,4,26, 27	C12Q1/68 C07H21/04 G01N33/574
Y	* the whole document * ---	2,3,6-9, 11,12	
X	WO 98 33450 A (PORTER PEGGY L ;ROBERTS JAMES M (US)) 6 August 1998 (1998-08-06)	1,4,26, 27	
Y	* abstract * * page 4, line 20 - page 5, line 6 * * claims 1-9 * ---	2,3,6-9, 11,12	
		-/-	
<p>The supplementary search report has been based on the last set of claims valid and available at the start of the search.</p> <p>INCOMPLETE SEARCH</p> <p>The Search Division considers that the present application, or some or all of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for the following claims:</p> <p>Claims searched completely :</p> <p>Claims searched incompletely :</p> <p>Claims not searched :</p> <p>Reason for the limitation of the search: see sheet C</p>			
7	Place of search	Date of completion of the search	Examiner
EPO FORM 1503 03/82 (P04C20)	MUNICH	7 October 2002	Madlener, M
CATEGORY OF CITED DOCUMENTS			
<p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	CORDON-CARDO C ET AL: "DISTINCT ALTERED PATTERNS OF P27 GENE EXPRESSION IN BENIGN PROSTATIC HYPERPLASIA AND PROSTATIC CARCINIMA" JOURNAL OF THE NATIONAL CANCER INSTITUTE, US DEPT. OF HEALTH, EDUCATION AND WELFARE, PUBLIC HEALTH, US, vol. 17, no. 90, 2 September 1998 (1998-09-02), pages 1284-1291, XP001080206 ISSN: 0027-8874	1-4,26, 27	
Y	* the whole document *	6-9,11, 12	
X	COTE RICHARD J ET AL: "Association of p27kip1 levels with recurrence and survival in patients with stage C prostate carcinoma." JOURNAL OF THE NATIONAL CANCER INSTITUTE (BETHESDA), vol. 90, no. 12, 17 June 1998 (1998-06-17), pages 916-920, XP002931303 ISSN: 0027-8874	1,4,26	
Y	* abstract *	6-9,11, 12	
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PARTIAL EUROPEAN SEARCH REPORT

Application Number
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DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	LLOYD RICARDO V ET AL: "p27Kip1: A multifunctional cyclin-dependent kinase inhibitor with prognostic significance in human cancers." AMERICAN JOURNAL OF PATHOLOGY, vol. 154, no. 2, February 1999 (1999-02), pages 313-323, XP002931302 ISSN: 0002-9440	1,4,26	
Y	* abstract * ---	6-9,11, 12	
X	GUO Y ET AL: "Loss of the cyclin-dependent kinase inhibitor p27(Kip1) protein in human prostate cancer correlates with tumor grade." CLINICAL CANCER RESEARCH: AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. UNITED STATES DEC 1997, vol. 3, no. 12 Pt 1, December 1997 (1997-12), pages 2269-2274, XP002916572 ISSN: 1078-0432	1,26	
Y	* abstract * * page 2273, last paragraph * ----	4,6-9, 11,12	
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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	MARZO DE ANGELO M ET AL: "Prostate stem cell compartments: Expression of the cell cycle inhibitor p27kip1 in normal, hyperplastic, and neoplastic cells" AMERICAN JOURNAL OF PATHOLOGY, PHILADELPHIA, PA, US, vol. 153, no. 3, September 1998 (1998-09), pages 911-919, XP002199162 ISSN: 0002-9440	1,26	
Y	* abstract * * page 918 *	4,6-9, 11,12	
X	FERNÁNDEZ P L ET AL: "Expression of p27/Kip1 is down-regulated in human prostate carcinoma progression." THE JOURNAL OF PATHOLOGY. ENGLAND APR 1999, vol. 187, no. 5, April 1999 (1999-04), pages 563-566, XP002199163 ISSN: 0022-3417	1,26	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	* abstract * * page 565 - page 566 *	4,6-9, 11,12	
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DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	MCARTHUR J G ET AL: "Cancer gene therapy with novel chimeric p27/p16 tumor suppressor genes." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, vol. 40, March 1999 (1999-03), page 630 XP002144030 90th Annual Meeting of the American Association for Cancer Research; Philadelphia, Pennsylvania, USA; April 10-14, 1999, March, 1999 ISSN: 0197-016X * the whole document * ---	6-9,11,12	
Y	CARIOU S ET AL: "PROGNOSTIC IMPLICATIONS OF EXPRESSION OF THE CELL CYCLE INHIBITOR PROTEIN P27" BREAST CANCER RESEARCH AND TREATMENT, NIJHOFF, BOSTON, US, vol. 1-3, no. 52, 1998, pages 29-41, XP001080251 ISSN: 0167-6806 * abstract * * page 37, right-hand column *	6-9,11,12	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	WO 94 22478 A (UNIV PENNSYLVANIA ; GREENE MARK I (US); KATSUMATO MAKOTO (US)) 13 October 1994 (1994-10-13) * abstract * * page 2, line 5 - line 17 * * page 3, line 13 - line 31 *	19-25	
P,X	WO 99 31140 A (GENENTECH INC) 24 June 1999 (1999-06-24) * abstract * * page 3, line 29 - page 4, line 37 * * page 27, line 12 - page 30, line 31 * * claims 1-19 *	19-25	

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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	AALTOMAA S ET AL: "Prognostic value and expression of p21(waf1/cip1) protein in prostate cancer." THE PROSTATE. UNITED STATES 1 APR 1999, vol. 39, no. 1, 1 April 1999 (1999-04-01), pages 8-15, XP002213568 ISSN: 0270-4137 * abstract * * page 9, right-hand column, paragraph 2 * * page 12, left-hand column, paragraph 2 * ---	14,28	
X	BARETTON G B ET AL: "Proliferation- and apoptosis-associated factors in advanced prostatic carcinomas before and after androgen deprivation therapy: prognostic significance of p21/WAF1/CIP1 expression." BRITISH JOURNAL OF CANCER. SCOTLAND MAY 1999, vol. 80, no. 3-4, May 1999 (1999-05), pages 546-555, XP002213569 ISSN: 0007-0920 * abstract * * page 552 - page 554 *	14,28	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	YAMASAKI ICHIRO ET AL: "Overexpression of MDM2 and p53 protein is infrequently but significantly associated with progression of human prostatic adenocarcinoma." ONCOLOGY REPORTS, vol. 3, no. 5, 1996, pages 925-929, XP002213570 ISSN: 1021-335X * abstract * * page 927, right-hand column - page 928 * ---	15,29	



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DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; March 1999 (1999-03) LEE TAE YOON ET AL: "Immunohistochemical expression of p53 and MDM-2 protein in various epithelial carcinomas." Database accession no. PREV199900406745 XP002213577 * abstract * & CHUNG-ANG JOURNAL OF MEDICINE, vol. 24, no. 1, March 1999 (1999-03), pages 1-11, ISSN: 0253-6250</p> <p>---</p>	15,29	
X	<p>HAN EDWARD KYU-HO ET AL: "Cyclin D1 expression in human prostate carcinoma cell lines and primary tumors." PROSTATE, vol. 35, no. 2, May 1998 (1998-05), pages 95-101, XP002213571 ISSN: 0270-4137</p> <p>---</p>	16,30	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	<p>* abstract * * page 99 *</p> <p>---</p>	17	
X	<p>GUMBINER LAURA M ET AL: "Overexpression of cyclin D1 is rare in human prostate carcinoma." PROSTATE, vol. 38, no. 1, 1 January 1999 (1999-01-01), pages 40-45, XP001105184 ISSN: 0270-4137</p> <p>---</p>	16,30	
Y	<p>* abstract * * page 44 *</p> <p>---</p>	17	
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DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	CHEN Y ET AL: "Increased cell growth and tumorigenicity in human prostate LNCaP cells by overexpression to cyclin D1." ONCOGENE. ENGLAND 16 APR 1998, vol. 16, no. 15, 16 April 1998 (1998-04-16), pages 1913-1920, XP002213572 ISSN: 0950-9232	16,30	
Y	* abstract * * page 1918 *	17	
X	--- LEE C T ET AL: "OVEREXPRESSION OF THE CYCLIN-DEPENDENT KINASE INHIBITOR P16 IS ASSOCIATED WITH TUMOR RECURRENCE IN HUMAN PROSTATE CANCER" CLINICAL CANCER RESEARCH, THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, US, vol. 5, no. 5, May 1999 (1999-05), pages 977-983, XP001016336 ISSN: 1078-0432 * abstract *	18,31	
X	--- CURNOW R T: "CLINICAL EXPERIENCE WITH CD64-DIRECTED IMMUNOTHERAPY. AN OVERVIEW" CANCER IMMUNOLOGY AND IMMUNOTHERAPY, BERLIN, DE, vol. 45, no. 3/4, November 1997 (1997-11), pages 210-215, XP000918956 ISSN: 0340-7004 * page 210 *	19,20	
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X	JAMES N ET AL: "PHASE II TRIAL OF THE BISPECIFIC ANTIBODY MDX-H210 (ANTI-HER2/NEU X ANTI-CD64) COMBINED WITH GM-CSF IN PATIENTS WITH ADVANCED PROSTATE AND RENAL CELL CARCINOMAS THAT EXPRESS HER2/NEU" BRITISH JOURNAL OF CANCER, LONDON, GB, vol. 78, no. SUPPL 2, 5 July 1998 (1998-07-05), page 19 XP000940750 ISSN: 0007-0920 * the whole document * ---	19-23	
X	ZHOU H E ET AL: "Expression of c-erb B-2/neu proto-oncogene in human prostatic cancer tissues and cell lines." MOLECULAR CARCINOGENESIS. UNITED STATES 1992, vol. 5, no. 4, 1992, pages 320-327, XP002213573 ISSN: 0899-1987	24,25	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	* abstract * * page 322 - page 326 * * figure 2 * ---	19-23	
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DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	VELTRI ROBERT W ET AL: "Quantitative nuclear morphometry, Markovian texture descriptors, and DNA content captured on a CAS-200 image analysis systems, combined with PCNA and HER-2/neu immunohistochemistry for prediction of prostate cancer progression." JOURNAL OF CELLULAR BIOCHEMISTRY SUPPLEMENT, no. 19, 1994, pages 249-258, XP002213574 ISSN: 0733-1959 * abstract * * page 256 * * table 3 * ---	24,25	
X	ROSS JEFFREY S ET AL: "Contribution of HER-2/neu oncogene expression to tumor grade and DNA content analysis in the prediction of prostatic carcinoma metastasis." CANCER (PHILADELPHIA), vol. 72, no. 10, 1993, pages 3020-3028, XP002214671 ISSN: 0008-543X * abstract * ---	24,25	
X	ARAI YOICHI ET AL: "C-erbB-2 Oncoprotein: A potential biomarker of advanced prostate cancer." PROSTATE, vol. 30, no. 3, 1997, pages 195-201, XP002214672 ISSN: 0270-4137 * abstract * --- -/-	24,25	



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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	KOENEMAN K S ET AL: "OSTEOMIMETIC PROPERTIES OF PROSTATE CANCER CELLS: A HYPOTHESIS SUPPORTING THE PREDILECTION OF PROSTATE CANCER METASTASIS AND GROWTH IN THE BONE ENVIRONMENT" PROSTATE, WILEY-LISS, NEW YORK, NY, US, vol. 39, 1999, pages 246-261, XP002946861 ISSN: 0270-4137 * abstract * ---	17	
Y	CRAFT NOAH ET AL: "A mechanism for hormone-independent prostate cancer through modulation of androgen receptor signaling by the HER-2/neu tyrosine kinase." NATURE MEDICINE, vol. 5, no. 3, March 1999 (1999-03), pages 280-285, XP002213575 ISSN: 1078-8956 * abstract *	19-25	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	BASELGA J ET AL: "RECOMBINANT HUMANIZED ANTI-HER2 ANTIBODY (HERCEPTIN TM) ENHANCES THE ANTITUMOR ACTIVITY OF PACLITAXEL AND DOXORUBICIN AGAINST HER2/NEU OVEREXPRESSING HUMAN BREAST CANCER XENOGRAFTS" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 58, no. 13, 1998, pages 2825-2831, XP000919190 ISSN: 0008-5472 * abstract *	20,21	
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DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
P,X	<p>OSMAN I ET AL: "Inactivation of the p53 pathway in prostate cancer: impact on tumor progression." CLINICAL CANCER RESEARCH: AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. UNITED STATES AUG 1999, vol. 5, no. 8, August 1999 (1999-08), pages 2082-2088, XP002213576 ISSN: 1078-0432 * abstract *</p> <p>---</p>	14-16, 28-30	
P,X	<p>AGUS D B ET AL: "RESPONSE OF PROSTATE CANCER TO ANTI-HER-2/NEU ANTIBODY IN ANDROGEN DEPENDENT AND -INDEPENDENT HUMAN XENOGRAFT MODELS" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 59, 1 October 1999 (1999-10-01), pages 4761-4764, XP000919490 ISSN: 0008-5472 * abstract * * page 4762 - page 4764 *</p> <p>-----</p>	19-25	TECHNICAL FIELDS SEARCHED (Int.Cl.7)



European Patent
Office

INCOMPLETE SEARCH
SHEET C

Application Number
EP 00 93 8256

Claim(s) searched completely:
1-4, 6-9, 11-12, 14-31

Claim(s) not searched:
5, 10, 13

Reason for the limitation of the search:

Present claims 5, 10 and 13 relate to substances defined by reference to desirable characteristics or properties, namely their capability of inducing p27 protein expression (claim 5) or their capability of stabilizing the p27 protein (claims 10 and 13).

Claims 5, 10 and 13 relate to all substances having one of these characteristics or properties, without relating to any further technical features. However, the application does not provide any according support within the meaning of Article 84 EPC and/or disclosure within the meaning of Article 83 EPC.

Moreover, and independent of the above reasoning, the claims also lack clarity (Article 84 EPC) for the reason that an attempt is made to define the substances only by reference to a result to be achieved (induction of p27 expression; stabilization of the p27 protein). The lack of any other technical feature does not allow the skilled person to clearly and unambiguously understand the scope of the claims. Again, this lack of clarity in the present case is such as to render a meaningful search impossible.

ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.

EP 00 93 8256

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

07-10-2002

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